

LF/(LF+HF) index in Ventricular Repolarization Variability correlated and uncorrelated with Heart Rate Variability

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Abstract—The purpose of this study, was to asses whether LF/(LF+HF) obtained from ventricular repolarization variability (VRV) reflects the state of sympathovagal balance. The VRV time series and Heart Rate Variability (HRV) time series from seventy two electrocardiogram (ECG) records in four different Autonomic Nervous System (ANS) profiles (athletes, cardiac transplant patient, heart failure patients and normal subjects) were extracted. A dynamic linear parametric model was applied to separate the VRV in two parts, VRV correlated with HRV (VRV_c) and VRV uncorrelated with HRV (VRV_u). Spectral indices were obtained from HRV, VRV, VRV_c and VRV_u time series. Changes of these indicators from rest to tilt position were analyzed. Results showed that: i) only LF/(LF+HF) from HRV time series increases significantly from rest to tilt in all ANS profiles, this information could not be retrieved in the other three series (VRV, VRV_c and VRV_u), ii) LF/(LF+HF) index in HRV series are significantly different between normal subjects and heart failure patients, while cardiac transplant patients show a low coherence between HRV and VRV power spectra and iii) HF rhythm in VRV series seem to be related to the mechanical effect of respiration.

I. INTRODUCTION

A great number of works have sought to establish relations between the variability of the ventricular repolarization (VRV) and heart rate variability (HRV). Peaks in the low frequency (LF) and high frequency (HF) bands were observed in the power spectra of the VRV and the HRV time series [1]. Additionally, it was found that the power distribution between LF and HF in the VRV power spectrum was reversed with respect to heart rate power spectrum. Generally, $LF/(LF+HF)_{HRV}$ is higher than 0.5 and $LF/(LF+HF)_{VRV}$ is smaller than this value. However, the physiological origins of these components are explained partially and the interpretation of the spectral parameters resulting from VRV sequence remains incomplete [2].

Moreover, a recent work using multiple correspondence analysis shows that low frequencies of the HRV and VRV

series were correlated [3]. In that work, high frequencies of the VRV space seem to be inadequate markers for the characterization of the Autonomic Nervous System (ANS). However, they observed that using only VRV parameters additional information from the population was obtained. These controversial results led us to explore a dynamic linear parametric model to quantify the dependence of ventricular repolarization variability to heart rate variability. This model allows separation of VRV series into a series correlated and uncorrelated with HRV [4]. The uncorrelation between VRV and HRV does not imply that there is not any physiological dependence between them [5].

In order to better understand the relationships between heart rate and ventricular repolarization phenomena, this model appears as an interesting tool to explore the value of the index LF/(LF+HF) in VRV correlated and VRV uncorrelated to HRV series.

The aims of this study were: i) to study LF/(LF+HF) of VRV from correlated and uncorrelated series, to reflect the state of sympathovagal balance in resting position, ii) to compare LF/(LF+HF) index in four different ANS profiles: athlete subjects, cardiac transplant patients, heart failure patients, and normal subjects.

II. METHODS

A. Model Formulation

The model was based on the one proposed by Porta et al. [4]. It analyzes the beat-to-beat series of the HRV series from the RR durations and VRV series from the RT apex (RT max) periods. From these two signals, a parametric identification procedure and spectral decomposition techniques allow to separate VRV series into VRV correlated to HRV series (VRV_c) and VRV uncorrelated to HRV series (VRV_u). The transfer function VRV-HRV can thus be determined (Figure 1).

A_{11} , A_{12} , A_{22} and D_1 are polynomials of order n in the z^{-1} domain. W_{HRV} and W_{VRV} are zero-mean white noises with variance λ^2_{HRV} and λ^2_{VRV} , respectively. The polynomial A_{22} can be estimated using a least squares approach, and the A_{11} , A_{12} and D_1 can be obtained using a generalized least squares (GLS) methodology [4, 5].

The model order n is chosen inside the set {8,10,12}, according to the minimum of the Akaike figure of merit [6]. As no a priori information was used, all blocks of the model are of the same order, thus, not giving an advantage to one

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mechanism with respect to the others.

From figure 1, two transfer functions can be identified. The first one, $H_1(z) = 1/(D_1(z)A_{11}(z))$, has as output the VRV uncorrelated to HRV (VRV_u), which is supposed to be the ANS action to the VRV. The second one, $H_2(z) = A_{12}(z)/(A_{22}(z)A_{11}(z))$, has as output the VRV correlated to HRV (VRV_r) and it is supposed to reflect the modulation of the HRV with respect to VRV.

RR series was modeled as a n order autoregressive (AR) stationary process given by equation 1, and VRV series, given by equations 2 and 3, was the result of two uncorrelated sources (ARARX model, [7])

$$HRV[i] = -\sum_{k=1}^n a_{22}[k]HRV[i-k] + W_{HRV}[i] \quad (1)$$

$$VRV[i] = \sum_{k=0}^n a_{12}[k]HRV[i-k] - \sum_{k=1}^n a_{11}[k]VRV[i-k] + N_{VRV}[i] \quad (2)$$

$$N_{VRV}[i] = -\sum_{k=1}^n d_1[k]N_{VRV}[i-k] + W_{VRV}[i] \quad (3)$$

Because of the uncorrelation between inputs W_{VRV} and W_{HRV} , the power spectral density of VRV (S_{VRV}) can be computed as the sum of the two partial power spectra that express the contribution of each source:

$$S_{VRV}(f) = S_{VRV_r}(f) + S_{VRV_u}(f) \quad (4)$$

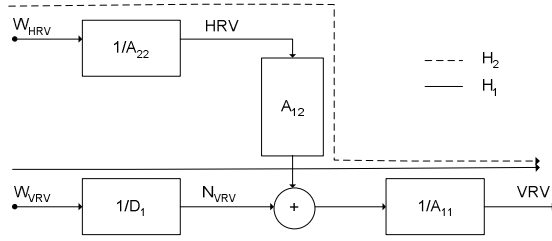


Fig. 1. Dynamic linear parametric model.

B. Study Population

In this work, seventy two subjects were studied. Each subject performed two tests with duration of five minutes each, as indicated below:

- Test 1 (rest): free ventilation in supine position.
- Test 2 (tilt): free ventilation in standing position.

Subjects belong to one of two protocols:

Protocol I: A database of thirty (30) young healthy subjects: 12 swimmers, 7 judokas and 11 sedentary, (20 ± 2 years of age) were analyzed. In total, sixty ECG records were analyzed.

Protocol II: A database of forty two (42) males subjects: 24 cardiac transplant patients (55.1 ± 6.7 years of age), 10 heart failure patients (62.1 ± 2.3 years of age) and 8 control subjects (64.0 ± 3.0 years of age) were analyzed. In total, eighty four ECG records were analyzed.

In total one hundred forty four (144) ECG records were analyzed from the two protocols.

C. HRV and VRV Series

HRV sequences were obtained using the Gritzali QRS detector followed by a manual verification of each detected R-wave [8]. VRV series were obtained by applying the algorithm proposed by Vila et al. [9]. Artifacts in the VRV sequence were also manually removed.

D. Spectral Analysis

The HRV and VRV sequences were linearly interpolated and uniformly sampled at 2 Hz. A time-varying autoregressive modeling of the interpolated HRV and VRV sequences was performed by using a 25 seconds sliding window. Power spectral densities were estimated. For each test the following parameters were determined: LF_{HRV} , HF_{HRV} , $LF/(LF+HF)_{HRV}$ for HRV sequences, and LF_{VRV} , HF_{VRV} , $LF/(LF+HF)_{VRV}$ for VRV sequences. The LF and HF bands were defined respectively by [0.04-0.15 Hz] and by [0.15-0.4 Hz] as proposed in [10].

E. Parametric Model

In order to illustrate, in a simple way, the operation of the model, it was validated using sine waves of frequencies corresponding to LF and HF components. Akaike criterion was used to fix the model order [6].

Tables I and II show mean coherence values of the power spectra between HRV and VRV series in LF and HF bands. The model was applied using criteria of a mean coherence value higher than 0.5.

TABLE I
THE COHERENCE FUNCTION FOR PROTOCOL I.

Subject	Rest		Tilt	
	K(LF)	K(HF)	K(LF)	K(HF)
Swimmers	0.69±0.28	0.62±0.21	0.75±0.21	0.69±0.23
Judokas	0.77±0.24	0.62±0.14	0.84±0.16	0.59±0.24
Sedentary	0.73±0.19	0.64±0.23	0.80±0.19	0.67±0.25

TABLE II
THE COHERENCE FUNCTION FOR PROTOCOL II.

Subject	Rest		Tilt	
	K(LF)	K(HF)	K(LF)	K(HF)
Cardiac transplant	0.67±0.24	0.56±0.19	0.65±0.22	0.50±0.22
Heart failure	0.72±0.25	0.72±0.15	0.77±0.18	0.68±0.15
Normal Subjects	0.81±0.16	0.61±0.17	0.65±0.13	0.66±0.19

From the model VRV_r and VRV_u were obtained, power spectral densities were estimated and, $LF(LF+HF)_r$ and $LF/(LF+HF)_u$ were determined.

III. RESULTS

Results are presented as mean \pm SD. Wilcoxon tests were used to determine the significance of the differences between rest and tilt, and between populations. A $p < 0.05$ is considered significant.

A. Spectral Analysis

The $LF/(LF+HF)_{HRV}$ and $LF/(LF+HF)_{VRV}$ values are

shown in tables III and IV for protocols I and II respectively.

TABLE III
LF/(LF+HF) VALUES FOR HRV AND VRV SEQUENCES IN THE REST AND TILT CONDITION FOR PROTOCOL I.

Subject	LF/(LF+HF) _{HRV}		LF/(LF+HF) _{VRV}	
	Rest	Tilt	Rest	Tilt
Swimmers	0.49±0.2	0.74±0.18	0.41±0.24	0.53±0.21
Judokas	0.49±0.23	0.84±0.1	0.37±0.24	0.53±0.17
Sedentary	0.52±0.16	0.68±0.22	0.42±0.08	0.47±0.19

TABLE IV
LF/(LF+HF) VALUES FOR THE HRV AND VRV SEQUENCES IN THE REST AND TILT CONDITION FOR THE PROTOCOL II.

Subject	LF/(LF+HF) _{HRV}		LF/(LF+HF) _{VRV}	
	Rest	Tilt	Rest	Tilt
Cardiac transplant	0.46±0.29	0.54±0.29	0.29±0.14	0.32±0.16
Heart failure	0.45±0.17	0.59±0.13	0.35±0.11	0.38±0.14
Normal Subjects	0.68±0.16	0.80±0.09	0.41±0.19	0.46±0.18

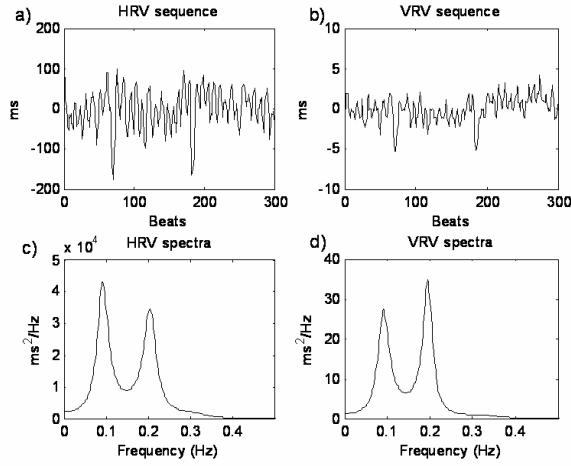


Fig. 2. Examples of: (a) HRV sequences, (b) VRV sequences, (c) HRV power spectra, and (d) VRV power spectra for a normal subject in resting position.

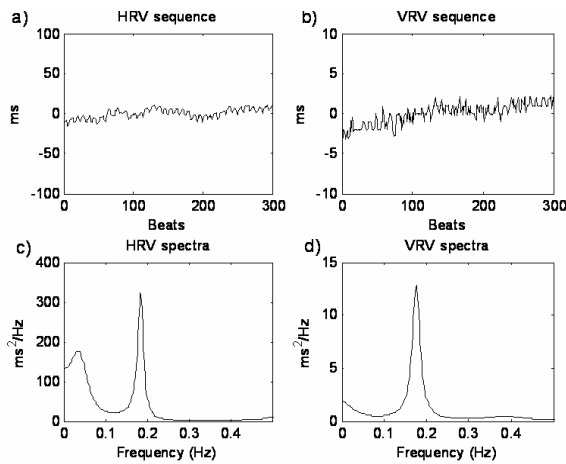


Fig. 3. Examples of: (a) HRV sequences, (b) VRV sequences, (c) HRV power spectra, and (d) VRV power spectra for a cardiac transplant patient in resting position.

LF/(LF+HF)_{HRV} increases significantly from rest to tilt in

both protocols and for all populations. In the case of LF/(LF+HF)_{VRV} no significant changes were observed. Also, in protocol II, LF/(LF+HF)_{HRV} allows to differentiate between populations, it is larger in control subjects than in heart failure patients ($p < 0.01$) (see table IV).

Figure 2 shows HRV and VRV sequences and power spectra for a normal subject resting position. Both power spectra confirmed that the HRV and VRV series exhibit LF and HF peaks.

Figure 3 shows HRV and VRV sequences and power spectra for a transplant cardiac patient in resting position. VRV spectrum is characterized by an prominent HF peak, LF component is minor.

B. Parametric Model

Results of LF/(LF+HF) values from the parametric model for protocols I and II are summarized in tables V and VI, respectively.

TABLE V
LF/(LF+HF) VALUES FOR VRV_r AND VRV_u SEQUENCES IN THE REST AND TILT CONDITION FOR THE PROTOCOL I.

Subject	LF/(LF+HF) _{VRVr}		LF/(LF+HF) _{VRVu}	
	Rest	Tilt	Rest	Tilt
Swimmers	0.59±0.22	0.66±0.29	0.44±0.23	0.41±0.24
Judokas	0.59±0.21	0.76±0.18	0.42±0.23	0.41±0.19
Sedentary	0.53±0.19	0.56±0.2	0.30±0.13	0.39±0.17

TABLE VI
LF/(LF+HF) VALUES FOR VRV_r AND VRV_u SEQUENCES IN THE REST AND TILT CONDITION FOR THE PROTOCOL II.

Subject	LF/(LF+HF) _{VRVr}		LF/(LF+HF) _{VRVu}	
	Rest	Tilt	Rest	Tilt
Cardiac transplant	0.31±0.25	0.33±0.27	0.29±0.12	0.31±0.12
Heart failure	0.31±0.22	0.36±0.27	0.39±0.16	0.36±0.13
Normal	0.47±0.28	0.57±0.23	0.33±0.15	0.35±0.16
Subjects				

No differences were observed neither in LF/(LF+HF)_r nor in LF/(LF+HF)_u when subjects changed from rest to tilt ($p > 0.05$).

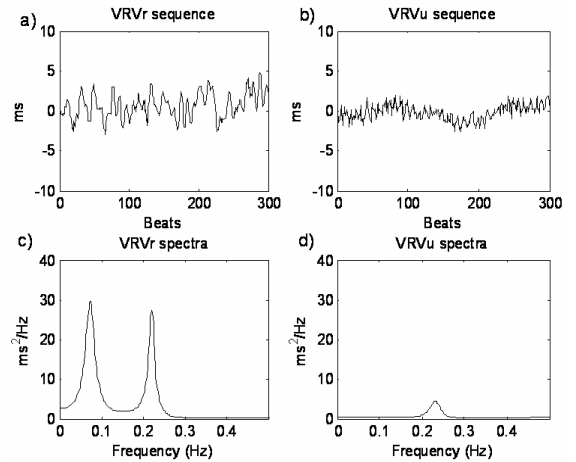


Fig. 4. Decomposition of the VRV for a normal subject: (a) VRV_r series, (b) VRV_u series, (c) VRV_r power spectra, and (d) VRV_u power spectra.

Figures 4 and 5 show the VRV decomposition: VRV_r , VRV_u series and power spectra, for a normal subject and a cardiac patient respectively. For both, cases VRV_r is more important, VRV_u seems to be negligible. Both power spectra are characterized by an important HF peak.

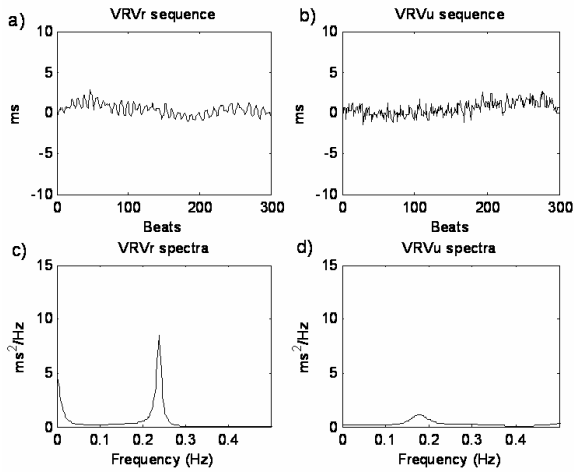


Fig. 5. Decomposition of the VRV for a cardiac transplanted patient: (a) VRV_r series, (b) VRV_u series, (c) VRV_r power spectra, and (d) VRV_u power spectra.

IV. DISCUSSION

The $LF/(LF+HF)_{HRV}$ has been proposed as an index to evaluate ANS condition. Results of this work confirm this fact as the $LF/(LF+HF)_{HRV}$ index provided significant differences between rest and tilt in four different ANS profiles: athlete subjects, cardiac transplant patients, heart failure patients, and normal subjects.

On the other hand, $LF/(LF+HF)_{VRV}$ is not a marker of sympathovagal balance. In VRV_r , we expected to find discriminant potential of $LF/(LF+HF)_{HRV}$, nevertheless, the dynamic decomposition did not reflect ANS balance. In VRV_r and VRV_u series, similar results for $LF/(LF+HF)$ were observed, but this index did not allow to separate between rest and tilt test. This behavior could be explained as follows: i) the fact that ventricular repolarization depends on heart rate and ANS, but also on humoral factors that are not taken into account in the parametric model. ii) HF oscillations in VRV series is not yet a fully understood issue. Porta et al. [4] concluded that VRV_u has its most important frequency components in the very low frequency band (VLF) and Wong et al. [3], reported that HF in VRV series has not physiological significance correlated to ANS regulation.

An important HF rhythm was observed in VRV sequences for all populations. This might explain the reversal power distribution between HRV and VRV, and stressed the difficulty of the interpretation of the physiological significance of $LF/(LF+HF)$ in VRV series. HF component could reflect the mechanical effect of respiration. Since in cardiac transplant patients, ANS efferent nerves are severed

during the surgical procedure, respiration seems to be the most important physiological source of HF component.

Low values of coherence observed in cardiac transplant patients show that the modulation of heart rate on ventricular repolarization is very low in this population. Control subjects must have a higher sensitivity of sinus node response to ANS than cardiac transplanted patients; however, non differences were found between these populations. This is because the large variance observed in cardiac transplant patient parameters. This variance is explained by the heterogeneous elapsed time after transplantation (60 ± 48 month) for this group.

Our findings are in agreement with previous studies [2, 3, 4, 11]. Where they have shown that most of the ventricular repolarization variability is due to the modulation of heart rate variability, LF components have better correlation than HF components (see tables I and II) and HF in VRV series reflects non neural mechanisms.

The model used in this work was proposed in the literature, nevertheless other techniques like standard prediction error tools would have been interesting to study.

Further research is needed to better understand repolarization ventricular phenomena. Adaptive identification modeling techniques is proposed as a step forward to explore VLF, LF and HF components.

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